UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,333	11/14/2003	Anastasia Khvorova	DHARMA 0100-US2	6379

23719 7590 05/05/2006

KALOW & SPRINGUT LLP
488 MADISON AVENUE
19TH FLOOR
NEW YORK, NY 10022

EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,333	KHVOROVA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 19-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8 and 19-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Those rejections set forth in the prior Office Action, but not repeated in the instant Office Action have been withdrawn in response to Applicant's amendment and/or arguments.

Claim Rejections - 35 USC § 112

3. Applicant's arguments with respect to claims 2-5 and 19 have been considered but are moot in view of the new ground(s) of rejection. Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2, and those claims dependent therefrom, claims 3-5, recite the phrase "(b) of claim 1 ***further*** **comprises,"** this phrase is vague and indefinite since it is unclear if the method recited in claim 2 as it relates to step (b) of the method recited in claim 1, actually limits or broadens the scope of claim 1. The method of claim 2 recites wherein step (b) further comprises, this suggests a step that is performed in addition to the step recited in claim 1. It appears that the method of claim 2 does not limit the non-target specific criterion recited in claim 1 to "applying at least on of Formulas I, II and IV-IX to said at least one candidate siRNA."

Claim 19 was amended to recite wherein the siRNA comprise sense strand sequences of 18-25 bases, this phrase is vague and indefinite since it is the examiner's understanding that an siRNA molecule comprises both a sense and antisense strand.

4. Claims 1-6, 8, 19-37 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record.

5. Applicant's arguments filed 3-13-06 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on pages 17-21 of the response filed 3-13-06.

The examiner agrees that First and Second points of Applicant's traversal set forth on pages 17-18 of Applicant's response.

The Third point of Applicant's traversal states that amending claim 2 to provide that the method requires the comparison of the results of a formula as applied to at least two siRNA and selecting the siRNA that has the higher score addresses the rejection set forth in the prior Office Action. However, it is noted that claim 1 does not require the application of non-target specific criterion to at least two-candidate siRNA. Claim 1 suggests that this can be accomplished merely by applying the at least one non-target specific criterion to only one candidate siRNA. As stated previously, Applicant's specification, specifically the formulas recited in claim 2 provide only relative information regarding the functionality of an siRNA.

In the Fourth point of Applicant's traversal, Applicants suggest that the there appears to be a misunderstanding of the invention, moreover Applicants argue that each of the individual criterion was determined and proven by bioinformatics techniques as described on pages 38-40 of the specification as filed. However, Applicants did not address the statements set forth on page 26, lines 18-29 of the specification as filed, wherein it is stated that :

> is, for instance, more stringent. Alternatively, it is conceivable that analysis of a sequence with a given formula yields no acceptable siRNA sequences (*i.e.* low SMARTscores™). In this instance, it may be appropriate to re-analyze that sequences with a second algorithm that is, for instance, less stringent. In still other instances, analysis of a single sequence with two separate formulas may give rise to conflicting results (*i.e.* one formula generates a set of siRNA with high SMARTscores™ while the other formula identifies a set of siRNA with low SMARTscores™). In these instances, it may be necessary to determine which weighted factor(s) (*e.g.* GC content) are contributing to the discrepancy and assessing the sequence to decide whether these factors should or should not be included. Alternatively, the sequence could be analyzed by a third, fourth, or fifth algorithm to identify a set of rationally designed siRNA.

This passage suggests that the criteria set forth in the specification as filed, and as recited in instant claims 2 and 19, do not represent ***a proven set of criteria*** as required for the rational design of an siRNA, since the application of one or more of these criteria may or may not give you the desired result, or even give you conflicting results, and re-analysis with another algorithm may be required, or furthermore re-analysis with a third, fourth, or fifth algorithm may be required to identify a set of rationally designed siRNA. The above passage suggests the potential need for further

experimentation in order to identify functional siRNA, wherein such guidance is beyond the scope of the instant disclosure.

Applicant's Sixth point of traversal, addresses the Examiner's concern that the specification is internally inconsistent. In particular Applicants state that although the specification indicates that for formulas VIII and IX, a SMARTscore of higher than 0 or 20 effectively selected a set of functional siRNAs, the passage that is directed to selecting hyperfunctional siRNAs is not limited to Formulas VIII and IX. It remains that this passage is confusing since Applicant's guidance for specifically choosing functional siRNA based upon the use of the SMARTSCORE™ (i.e. Formulas VIII and IX, as stated above) siRNA ranking is not adequately described in the specification, i.e. if the SMARTSCORE method is be best mode of operating the claimed method, then the formula or its method of practice should be disclosed in the specification as filed.

Due to the lack of clear guidance set forth in the specification as filed that for selecting functional and hyperfunctional siRNA according to the present invention, the skilled artisan would not have been able to practice the full scope of the claimed invention without undue experimentation since the skilled artisan would have to resort to unpredictable *de novo* experimentation without particular guidance from the specification as filed. There are a variety of suggestions given regarding the evaluation of particular non-target specific criterion, however the skilled artisan is not given clear and specific guidance as how to use these particular criteria for rationally designing a functional or hyperfunctional siRNA. Moreover, apart from further experimentation,

without particular guidance from the specification as filed, there is no clear guidance for the selecting the particular criteria necessary for the rational design of siRNA.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1-6, 8, and 19, 21-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written Description).

Applicant's arguments have been fully considered, but are not persuasive. Applicants traversed the instant rejection on the grounds Applicants have adequately described both the use of non-target specific criterion and the specific criteria delineated in the specification are inventive. However, it is noted that the instant claims (with the exception of claim 19) are not limited to those specific criteria recited in the specification. As stated in the prior Office Action, Applicant's own specification suggests that other criteria, not specifically disclosed are encompassed within the scope of the invention, for example at page 40, criteria I-VIII are described, however at lines 27-29, it states that "in an effort to improve selection further, all identified criteria, ***including but not limited to those listed in Table IV*** were combined into algorithms embodied in Formula VIII, and Formula IX." There are so many permutations to these formulas, it is unclear what other specific proven criteria Applicants are referring to,

again, apart from further experimentation the skilled artisan would not be able to specifically pinpoint the particular parameter in these formulas that would be particularly useful for identifying the full scope of functional siRNA encompassed by the claims.

The instant claims are rejected for the reasons of record, and furthermore the instant claims are considered to lack a sufficient written description regarding the application of a "proven set of criteria that enhance the probability of identifying a functional or hyperfunctional siRNA." Due to the ambiguity associated with the disclosure (see pages 26, 40-41 and 53) regarding which particular criteria would yield the rationally designed siRNA according to the present invention, and the apparent need for further experimentation to identify the full scope of non-target specific criteria encompassed by the instant claims, it does not appear that Applicant's were in possession of the full scope of the invention at the time of the instant invention.

Applicants have amended claim 19 to recite wherein the first and second optimized siRNA comprise sense strand sequences of 18-25 bases, however there is no description provided regarding the antisense strand of the optimized siRNA molecules. It is unclear if the optimized siRNA comprise an antisense strand that is exactly complimentary to the sense strand, and is of exact length, or if the antisense strand comprises an overhang. Moreover, it is unclear if the optimized siRNA represent functional or hyperfunctional siRNA.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford
Primary Examiner
Art Unit 1633

JLE